IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

**Applicant:** Julio L. Pimentel

**Title:** Decreased Fat Absorption with an Anti-Lipase Antibody

**Serial No.:** 08/888,202

**Filed:** July 7, 1997

**Examiner:** Ungar

**Group Art Unit:** 1642


#16

4-Ub-00

## SUPPLEMENTAL DECLARATION UNDER 37 CFR §1.132

**Commissioner of Patents & Trademarks**
**Washington, D.C. 20231**

I, Richard Lee Atkinson, Jr., M.D., do hereby declare as follows:

(1) I have read the Office Action identified as Paper No. 13 and have reviewed the references relied upon by the Examiner in support of the rejection of claims.

(2) In my prior Declaration of August 6, 1999, I considered each of those references (except for the newly-cited Sterling reference) and stated why I considered them to be in non-analogous fields so that one skilled in the art would not be expected to combine them in the manner proposed by the Examiner. While I remain of that view, I will nevertheless respond to the latest Action, and to prior Actions, as if all of the references were properly combinable as asserted by the Examiner.

(3) As stated on pages 4 and 5 of my earlier Declaration, before I read the specification and claims of the present application (08/888,202), I would have been skeptical that lipase antibodies introduced orally into the gastrointestinal tract of post-newborn non-ruminant mammals would have any significant effect in inhibiting pancreatic lipase activity. The teachings of all of the references of record, taken in combination, would not have led me to a different conclusion, and I do not believe others skilled in the art would have considered the claimed invention to be obvious from the combined teachings of such references for the reasons set forth below.

(4) As previously stated, gastric acid and protein digestive enzymes in a post-newborn or post-suckling non-ruminant mammal would be expected to destroy antibodies before they reach the point in the digestive tract where pancreatic lipase enters. I do not find that the references of record disclose or suggest otherwise.

(5) The Hadvary patent (4,598,089) is relied upon by the Examiner as a main reference with which up to a total of nine other references are combined. The Hadvary patent concerns the use of tetrahydrolipstatin, now widely known under its trade name Xenical, which is a molecule clearly different and completely unrelated to avian-derived pancreatic lipase antibodies. If anything, Hadvary directs the reader away from the oral administration of antibodies for reducing fat absorption in a recipient, much less a healthy, post-suckling, non-ruminant mammallian recipient.

(6) The secondary references do disclose that antibodies may be administered to mammals for

various purposes, but those references fail to make up for Hadvary's shortcomings for one or more of a number of reasons. The Moloney, Flint, Ohkaru and Japanese (02150294) references are concerned with procedures in which antibodies are administered intravenously, subcutaneously, or intraperitoneally, but I do not find of them disclosing or suggesting that antibodies might be effectively administered orally. While the effect of antibodies inhibiting lipase activity is well known, I believe it is surprising and unexpected that such activity would be retained if the antibodies were orally administered to a healthy adult non-ruminant mammal, and I find nothing in these references to the contrary.

(7) It is also well known that antibodies in a mother's milk are capable of traveling through the digestive tract of nursing offspring and of retaining their activity in the not yet fully developed digestive systems of such offspring. The Tokoro and Martin et al references disclose oral administration of antibodies to mammals in the suckling period of post natal development. While it is not surprising that such antibodies retain activity in such young mammalian subjects, these references are not concerned with the treatment of older mammals and do not indicate that lipase antibodies would retain their effectiveness if orally administered to healthy post-suckling mammals.

(8) While the Perryman et al and Sterling et al references do refer to the treatment of adult mammals, in those cases the mammals have their digestive processes disrupted by intestinal parasitosis. Specifically, in Perryman et al the adult scid mice are persistently infected with C. parvum which may disrupt the normal operation of the animals' digestive systems, and in the Sterling et al reference the patentees describe treating intestinal parasitosis caused by C. parvum in mammals in need of such treatment. Neither reference discloses or suggests that different antibodies, particularly antibodies having a specificity for a normally-produced enzyme (pancreatic lipase), would be able to pass through the digestive tract of a healthy adult mammal and retain enzyme-inhibiting binding capabilities.

(9) I also note that the Sterling et al reference, while mentioning the treatment of adult subjects, only offers examples of the treatment of pathological conditions in newborn mice.

(10) The Coleman patent is concerned with the treatment of diseases in ruminant animals, specifically with the use of antibodies against some of the pathogens that cause mastitis in cattle. I find nothing in the Coleman patent that would lead one skilled in the art to believe that a natural enzyme, pancreatic lipase, could be inactivated by antibodies fed orally to a healthy, post-suckling non-ruminant mammmal.

(11) Therefore, even if all of the references relied upon by the Examiner were properly combinable, which I do not agree to be the case, I would still find it surprising and unobvious from their combined teachings that the production of pancreatic lipase in a post-suckling non-ruminant mammal could be inhibited by orally feeding that mammal avian-derived pancreatic lipase antibodies.

I affirm that the statements above are true to the best of my knowledge and belief, and I am aware that any false statements herein may subject me to penalties for purjury and may jeopardize the validity of any patent or patents that may issue on the subject patent application.

Dated: March 30, 2000

Richard L. Atkinson, Jr., M.D.

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